

R' is selected from the group consisting of H, alkyl, and aryl, wherein said alkyl is optionally substituted with a six-membered heteroaliphatic ring, and wherein said six-membered ring is optionally substituted at one or more positions with substituents selected from the group consisting of alkyl, alkoxy, halogen, trihalomethyl, NO<sub>2</sub>, and (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R;

- b) measuring the activity of VEGF, FGF, or PDGF; and
- c) comparing said activity of VEGF, FGF, or PDGF to cells that have not been contacted with one more compounds of formula I.

### REMARKS

#### Status of the Claims

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim 16 is requested to be cancelled. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner.

Claims 1, 2, 8, 12, 14, 15 and 17 are currently being amended.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 1 and 2 are amended simply to correct clerical errors. Exemplary support for "4,5, 6,7-tetrahydroindole" and "1,2,3,5-thiatriazole" is found in the specification on page 25 and in originally filed claim 1. It is obvious from the context of the specification and to those of skill in the art that "1,3,4-thiadaizole" should be "1,3,4-thiadiazole." Support for "pyrrole" is found in the specification on page 25, line 10. Exemplary support for the amendments to claim 8 is found in the specification on page 5, lines 1-24. Exemplary support for the

amendments to claim 12 is found in the specification on page 5, lines 1-24; page 24, lines 6-9; and page 93, line 18, through page 97, line 25. In claim 15, the phrase “1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadaizole” was amended to recite “1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole” because of clerical errors.

Upon entry of this Amendment, claims 1-15 and 17 will remain pending in the application, with claims 1-7 withdrawn from consideration as a result of a Restriction Requirement and claims 8-15 and 17 ready to be examined on the merits.

### **Issues Under Priority**

The Examiner asserts that the claims only have priority to June 5, 1996, and not June 7, 1995 as claimed by Applicants, because there is allegedly no support for the A group defined in the instant invention in USP 5,880,141 (Application No. 08/485,323). Applicants respectfully disagree and assert that the correct priority date of the present application is June 7, 1995.

Formula I of the present invention is disclosed in the ‘141 patent at column 6, line 45, through column 7, line 25. In the ‘141 patent, substituent “R<sub>1</sub>” corresponds to substituent “A” in Formula I of the present application. The ‘141 patent states:

*“R<sub>1</sub> is a 5 or 6 membered mono- or bicyclic aryl or heteroaryl, substituted or unsubstituted ring wherein the preferred substituents are N-alkyl, C-alkyl, nitro, sulfonyl, hydroxy, alkoxy, halo, trihalo methyl, carboxy, carboxamide, amide, sulfonamide, H and cyano”*

In the present application, A is “selected from the group consisting of 4,5,6,7-tetrahydroindole, thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, 2-sulfonylfuran, 4-alkylfuran, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadaizole, 1,2,3,4-thiatriazole, 1,2,3,5-thiatriazole, and tetrazole, wherein said group is optionally substituted with one or

more substituents selected from the group consisting of alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO<sub>2</sub>NRR', SO<sub>3</sub>R, SR, NO<sub>2</sub>, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R, CONRR', and (CH<sub>2</sub>)<sub>n</sub>ONRR'."

The '141 patent provides a generic disclosure of R<sub>1</sub> substituents. Additionally, at column 5, lines 23-29 of the '141 patent, a description of "heterocyclic aryl" is provided:

*"'Heterocyclic aryl' refers to groups having from 1 to 3 heteroatoms as ring atoms in the aromatic ring and the remainder of the ring atoms are carbon atoms. Suitable heteroatoms include oxygen, sulfur, and nitrogen, and include furanyl, thienyl, pyridyl, pyrrolyl, N-lower alkyl pyrrolo, pyrimidyl, pyrazinyl, imidazolyl and the like, all optionally substituted.*

All of the compounds from which A is selected in the present application are encompassed by the disclosure of the '141 patent. A person of ordinary skill in the art would have recognized that Applicants possessed the A group, as claimed, as of the priority date. All of the compounds from which A is selected in the present application are envisioned by the disclosure of the '141 patent. Because the '141 patent has support for the compounds of the present application, the priority date of the present application is June 7, 1995, the filing date of the '141 patent.

### **Claim Objections**

Claim 16 is objected to by the Examiner under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 14. Applicants do not agree with the Examiner. However, in order to expedite prosecution, Applicants have canceled claim 16. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner.

### **Claim Rejections - 35 U.S.C. § 112, Second Paragraph**

Claims 8-17 are rejected by the Examiner under 35 U.S.C. § 112, second paragraph as being allegedly indefinite. Applicants respectfully request reconsideration and withdrawal of the rejection.

A) The Examiner asserts that claims 8-13 are indefinite because the R groups are not defined. Applicants have amended the claims in accordance with Formula I presented in claims 14-17, as suggested by the Examiner.

B) The Examiner asserts that claims 14-17 are indefinite because the claims do not set forth the relationship between the inhibition of VEGF, FGF or PDGF stimulated cell proliferation and vein endothelial cells or smooth muscle cells and the administration of one or more of the compounds of Formula I. Applicants have amended claims 14-17 to set forth the relationship. Support is found throughout the specification and in the examples.

C) The Examiner maintained the rejection of claims 12-13 as being indefinite because of the term “general disease symptoms.” Applicants do not agree with the Examiner. However, to expedite prosecution, Applicants have replaced the phrase “monitoring an effect upon general disease symptoms in said rats” in claim 12 with “monitoring in said rats one or more effects selected from the group consisting of ear nodulation, tail nodulation, nose swelling, paw swelling and ballanitis.” Exemplary support for the amendment to claim 12 is found in the specification on page 24, lines 6-9 and page 93, line 18, through page 97, line 25. Exemplary support for the amendments to claim 14, 15 and 17 is found in Examples 2, 3 and 5.

**Claim Rejections - 35 U.S.C. § 112, First Paragraph**

Claim 15 is rejected by the Examiner under 35 U.S.C. § 112, first paragraph for lack of enablement. Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner asserts that while the specification is enabling for treating arthritis in a patient by administering one or more compounds of Formula I, it allegedly does not provide enablement for treating or preventing endometriosis, ocular neovascularization, solid tumor growth and metastases, and excessive scarring during wound healing. Applicants do not agree with the Examiner’s assertion. However, to expedite prosecution, Applicants have amended claim 15 to be directed to a method for treating arthritis. Applicants reserve the right to pursue the deleted subject matter in subsequent divisional applications.

**Claim Rejections - 35 U.S.C. § 102**

Claims 14 and 16 are rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Sircar et al. (USP 5,389,661; issued 2/14/95). The Examiner asserts that the method of Sircar would appear to necessarily result in the same effect of inhibiting VEGF, FGF or PDGF since the method of Sircar includes each of the method steps of the presently claimed invention, i.e., the step of administering to a patient the chemical compound of formula I. Applicants respectfully request reconsideration and withdrawal of the rejection.

Applicants have canceled claim 16, thus rendering the rejection of this claim moot.

With respect to claim 14, as discussed above, the present invention is entitled to a priority date of June 7, 1995. Therefore, Sircar et al. is not 102(b) prior art against the present application.

While the Examiner has not rejected claim 14 under 35 U.S.C. § 102(e) as being anticipated by Sircar et al., Applicants take this opportunity to explain why amended claim 14 is not anticipated by Sircar et al. under 35 U.S.C. § 102(e). Applicants have deleted "imidazole" from the list of substituents that A can be in the compound of Formula I. The compounds disclosed in Sircar et al. are distinct from the compounds of claim 14 because the Sircar et al. compounds all have an imidazole group at the location in the molecule corresponding to "A" in the compounds of Formula I of claim 14. Because Sircar et al. discloses administering the Sircar et al. compounds for treating congestive heart failure and fails to disclose administering the compounds of claim 14, claim 14 is not anticipated by Sircar et al.

**CONCLUSION**

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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